

REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: FLORAS 50 SC

Product name(s): Floras 50 SC, HerbiFlo 50 SC

Chemical active substance:

Florasulam, 50 g/L

Central

Zonal Rapporteur Member State: POLAND

CORE ASSESSMENT

(authorization)

Applicant: Elvita Sp. z o.o.

Submission date: 30/11/2023, updated April 2024

MS Finalisation date: April 2024 (initial Core Assessment)

June 2024 (final Core Assessment)

Version history

When	What
November 2023	Applicant submission
March 2024	Applicants' update.
April 2024	<p>Initial assessment by the zRMS</p> <p>The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are struck through and shaded for transparency.</p>
June 2024	<p>Final report (Core Assessment updated following the commenting period)</p> <p>No additional information or assessments after the commenting period.</p>

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Reviewer general comment:

This part of dossier summarizes data related to the toxicological profile and NDE assessment for the plant protection product Floras 50 SC (HerbiFlo 50 SC identical plant protection product, different trade name) containing 50 g/L florasulam, Suspension Concentrate, which has been submitted to support registration according art. 33 of 1107/2009 in Poland also for zonal registration for which PL was designated zRMS. Intended use of PPP is as herbicide in the protection of cereal. The zRMS's review considers all the elements that are crucial for risk assessment and decision-making. Regarding evaluation of the toxicity potential (product Floras 50 SC) data submitted by the Applicant has been based on additivity calculation method (ATEmix; for details of calculations refer Part C) and *in vitro* studies.

zRMS Reviewer do not accept exposure assessment provided by the Applicant due to numerous incorrect assumptions made by the Notifier, therefore NDE assessment for operator, workers and B&R has been calculated by zRMS considering EFSA calculator, on-line version OPEX version: 1.0.2 (refer Appendix 5) and taking into account the worst-case exposure scenario to cover all the intended uses (highest application rate per application as well as the highest application rate per year with the shorter interval between each application). All NDE calculations for operator, workers and B&R resulting from use of PPP, considering all tasks according to the critical use(s), identify safe use of the product Floras 50 SC.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on Floras 50 SC *

Product name and code	Floras 50 SC
Formulation type	Suspension Concentrate; SC
Active substance(s) (incl. content)	Florasulam; 50 g/L
Function	Herbicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of Floras 50 SC can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1-2: Justified proposals for classification and labelling for Floras 50 SC according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	-
Hazard pictograms or Code(s) for hazard pictogram(s):	GHS09
Signal word:	Warning*
Hazard statement(s):	H410*
Precautionary statement(s):	P261 P273 P391 P501
Additional labelling phrases:	To avoid risks to man and the environment, comply with the instructions for use. [EUH401] Contains 1,2-Benzisothiazolin-3-one. May produce an allergic reaction [EUH208]

* **zRMS Reviewer comment:** this hazard statement is not properly included in part B6. This phrase is used to refer to the environmental hazard assessment (Hazardous to the aquatic environment) not for mammalian, therefore it has been removed from Table 6.1 2.

Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for Floras 50 SC.

	Result	PPE / Risk mitigation measures
Operators	Acceptable	AOEM: PPE (working wear and gloves) Operator wearing workwear but no gloves (M,L&A)
Workers	Acceptable	AOEM: PPE (working wear and gloves) Worker wearing workwear, long sleeved shirt, long trousers (“permeable”) but no gloves (inspection, irrigation)
Bystanders	Acceptable	AOEM None
Residents	Acceptable	AOEM BREAM* None

***zRMS Reviewer:** Mentioned model is not BREAM but BBA. Model BBA is no longer accepted

No unacceptable risk for operators, workers, bystanders and residents was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in are applied.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and bystanders/residents is presented in the following table.

Table 6.1-4 Critical uses and overall conclusion of exposure assessment

Table 6.14 Critical uses and overall conclusion of exposure assessment												
1	2	3	4	5	6	7	8	9	10			
Use-No.*	Crops and situation (e.g. growth stage of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Application		Application rate		PHI (d)	Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, bystander or resident exposure based on [Exposure model]	Acceptability of exposure assessment			
			Method / Kind (incl. application technique ***	Max. number (min. interval between applications)	Max. application rate kg as/ha a) Florasulam	Water L/ha min / max			Operator	Worker	Bystander	Residents
1	Winter wheat (BBCH 12-32)	F	Foliar spraying, FCTM	1 ; -	a) 0.005	<div>100 200- 400</div>	-					
2	Spring barley	F	Foliar spray-	1 ; -	a) 0.005	<div>100</div>	-					

1	2	3	4	5	6	7	8	9	10
	(BBCH 12-32)		ing, FCTM			200 - 400			

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 “Acceptability of exposure assessment”

A	Exposure acceptable without PPE / risk mitigation measures
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable/ Evaluation not possible

Noticed data gaps are:

None.

6.2 Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in

Table 6.2-1.

Table 6.2-1: Information on active substance(s)

Florasulam	
Common Name	2',6',8-trifluoro-5-methoxy[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide
CAS-No.	145701-23-1
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories: Aquatic Acute 1; H400 Aquatic Chronic 1; H410 Code(s) for hazard pictogram(s): GHS09 Signal word: Warning Hazard statement(s): H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects Precautionary statement(s): P273 Avoid release to the environment P311 Call a POISON CENTER /doctor P501 Dispose of contents/container to an approved waste disposal plant
Additional C&L proposal	-
Agreed EU endpoints	
AOEL systemic	0.05 mg/kg bw/d
Reference	EFSA Journal 2015;13(1): 3984
Conditions to take into account/critical areas of concern with regard to toxicology	
Review Report/EFSA Conclusion for active substance	Conditions of use include the application of adequate personal protective equipment, where appropriate.

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for Floras 50 SC is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for product Floras 50 SC

zRMS Reviewer comment:

****Regarding study “*Floras 50 SC: Use of the 3T3 neutral red uptake cytotoxicity test to estimate starting doses for acute oral systemic toxicity tests*”** Krakowian D., 2022, Reviewer would like indicate that protocol OECD 129 has several limitations are largely due to the differences between whole animal and cell culture systems. Animal and cell culture systems are different with respect to how a substance or toxicant is delivered to the cell and how it is distributed within the cell, metabolized, and excreted. After oral administration, animals must absorb the toxicant from the gastrointestinal tract. The toxicant may or may not be bound to serum proteins, which would reduce its availability to the target organ. The toxicant may be metabolized before, during, and/or after its distribution to the target organs, or the toxicant or its metabolites may be excreted before reaching the target organ. As a consequence, the most critical target organs may not be exposed to the active metabolite, or be exposed for only a limited time or to a relatively small fraction of the administered dose. If a toxicant acts in a specialized organ system *in vivo*, it may not produce a toxic effect by the same mechanism in cultured cells that are derived from a tissue different from the target organ. For example, a substance that affects a neuroreceptor-mediated pathway in animals would not be expected to produce a similar toxicity in 3T3 or NHK cells; if toxicity is seen in these cell cultures, it may be from a different mechanism or in a different concentration relationship than *in vivo*. Therefore study has not been accepted and for this endpoint (oral acute toxicity) assessment has been provided based on additivity method ATEmix.

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral, rat Acute Tox. (OECD 129) 3T3 neutral red uptake cytotoxicity test	No prediction can be made on oral acute toxicity**	No	--	Krakowian D., 2022
LD ₅₀ oral, rat Additivity method ATEmix	ATEmix = 1 000 000	Yes	None	Refer to Part C
LD ₅₀ dermal, rat Additivity method ATEmix	None of the ingre- dients is classified for dermal toxicity	Yes	None	Refer to Part C
LC ₅₀ inhalation, rat Additivity method ATEmix	None of the ingre- dients is classified for inhalation tox- icity	Yes	None	Refer to Part C
Skin irritation <i>In Vitro</i> OECD Guideline No. 431 (RhE)	Non-irritant	Yes	None	Krakowian D., 2022
Skin irritation Based on ingredient content	Non-irritant	Yes	None	Refer to Part C
Eye irritation, <i>In Vitro</i> OECD Guideline No. 438 ICE	Non-irritant	Yes	None	Gruszka K., 2022.
Eye irritation, Based on ingredient content	Non-irritant	Yes	None	Refer to Part C
<i>In Vitro</i> Skin Sensitisation (OECD 442D)	Non-sensitising	Yes	None	Krakowian D., 2022
<i>In Vitro</i> Skin Sensitisation (OECD 442E)	Non-sensitising	Yes	None	Krakowian D., 2023
Skin Sensitisation Based on ingredient content	Non-sensitising	Yes	None	Refer to Part C
Supplementary studies for combinations of plant protection products	No data – not required	--	--	--

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ -oral, rat	Not submitted, not necessary. Justification presented in Appendix 2			
Acute Tox. (OECD 129)	No acute tox.		None	Krakowian D., 2022
LD ₅₀ -dermal, rat	Not submitted, not necessary. Justification presented in Appendix 2			
LC ₅₀ -inhalation, rat	Not submitted, not necessary. Justification presented in Appendix 2			
Eye Irritation or Serious Eye Damage (OECD 438)	No		None	Gruszka K., 2022
In-Vitro Skin Corrosion (OECD 431)	No		None	Krakowian D., 2022
In-Vitro Skin Sensitisation (OECD 442D)	No		None	Krakowian D., 2022
In-Vitro Skin Sensitisation (OECD 442E)	No		None	Krakowian D., 2023
Skin sensitisation, guinea-pig	Not submitted, not necessary. Justification presented in Appendix 2			
Supplementary studies for combinations of plant protection products	No data—not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of Floras 50 SC

	Substance (Concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification of product (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of active substance(s) (relevant for classification of product)	Florasulam (0,56 % (w/w))	Aquatic Acute 1; H400 Aquatic Chronic 1; H410	Reg. 1272/2008	Not relevant
Toxicological properties of non-active substance(s) (relevant for classification of product)	Considered confidential, can be found in the confidential dossier of this submission (Registration Report - Part C)			
Further toxicological information	No data – not required	-	-	-

6.4 Toxicological Evaluation of Groundwater Metabolites

The following data on metabolites with the potential to reach the groundwater in concentrations above 0.1 µg/L and requiring relevance assessment were submitted. Note that the relevance assessment of the metabolites is reported in Part B.10; the submitted toxicological studies are summarized in this document.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in Floras 50 SC are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in Floras 50 SC

	Floras 50 SC	
	Value	Reference
Concentrate	25 10%	Guidance on dermal absorption. EFSA Journal 2017;15(6);4873.

	Floras 50 SC	
	Value	Reference
Dilution	75 50 %	

6.5.1 Justification for proposed values

No data on dermal absorption for active substance in Floras 50 SC are available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) are presented in the following table.

Table 6.5-2: Default dermal absorption rates

	Value	Justification for value	Acceptability of justification
Concentrate	25 10 %	Due to absence of any supporting dermal absorption studies for Floras 50 SC and based on Guidance on dermal absorption (EFSA Journal 2017; 15(6); 4873), default values are proposed (regarding type of formulation of Floras 50 SC): - 25 10 % for concentrate - 75 50 % for diluted product.	See zRMS comment below the table.
Dilution	75 50 %		

zRMS Reviewer comment: Default values of dermal absorption proposed by the Applicant for PPP Floras 50SC has been incorrectly entered. Based on Guidance on Dermal Absorption (EFSA Journal 2017;15(6)4873) for concentrate and spray dilution it must be 10% and 50% respectively (Formulation types: soluble concentrate (SL), suspension concentrate (SC), flowable concentrate for seed treatment (FS), flowable (FL) (=SC)). Due to Applicants mistake, zRMS decided to provide new NDE assessment.

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

Table 6.6-1: Product information and toxicological reference values used for exposure assessment

Product name and code	Floras 50 SC
Formulation type	SC
Category	Herbicide
Container size(s), short description	Bottle (HDPE): 120 ml, 250 ml, 500 ml, 1 ltr, Canister (HDPE): 5 ltr, 10 ltr, 20 ltr Drum (HDPE): 220 ltr IBC container (HDPE): 1 m ³
Active substance(s) (incl. content)	Florasulam 50 g/L
AOEL systemic	0.05 mg/kg bw/d (Florasulam)
Inhalation absorption	100 %
Oral absorption	100 %
Dermal absorption	Concentrate: 25 10% Dilution: 75 50% (Default values)

6.6.1 Selection of critical use(s) and justification

The critical GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the zone/ EU is given in Part B, Section 0.

6.6.2 Operator exposure (KCP 7.2.1)

zRMS Reviewer comment:

Reviewer do not accept exposure assessment provided by the Applicant due to numerous incorrect assumptions made by the Notifier, therefore NDE assessment for operator, workers and B&R has been calculated by zRMS considering EFSA calculator, on-line version OPEX: 1.0.2 also taking into account the worst-case exposure scenario to cover all the intended uses (highest application rate per application as well as the highest application rate per year with the shorter interval between each application). All NDE calculations provided for operator, workers and B&R resulting from use of PPP, considering all tasks according to the critical use(s), identify safe use of the product Floras 50 SC.

It must be noted that mentioned by the Applicant model BREAM is not BREAM, this is model BBA. Model BBA used for B&R assessment has not been accepted. Model is no longer valid for risk assessment.

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of Floras 50SC (HerbiFlo 50SC) according to the critical use(s) is presented in Table 6.6-8. Outcome of the estimation is presented in Table 6.6-9. Detailed calculations are in Appendix 35.

Table 6.6.2-2: Exposure models for intended uses

Critical use(s)	Winter wheat; Spring barley (max. 0.1L /product/ha)
Model(s)	EFSA on-line calculator OPEX version: 1.0.2

Table 6.6.2-3: Estimated operator exposure

Table 6.6.2.3: Estimated operator exposure			
		florasulam	
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Tractor mounted boom spray application outdoors to low crops Application rate:0.005 kg a.s./ha			
EFSA on-line calculator OPEX version: 1.0.2/ 75 th percentile) No drift reductio Body weight: 60 kg	no PPE*	0.008	16.6
	Workwear	0.006	12

* no PPE: Operator wearing T-shirt and shorts

6.6.3 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.4 Worker exposure (KCP 7.2.3)

6.6.4.1 Estimation of worker exposure

Table 6.6-10 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with Floras 50SC (HerbiFlo 50SC) according to the criti-

cal use(s). Outcome of the estimation is presented in Table 6.6-11. Detailed calculations are in **Appendix 35**.

Table 6.6.4-4: Exposure models for intended uses

Critical use(s)	Winter wheat; Spring barley (max. 0.1L /product/ha)
Model	EFSA on-line calculator OPEX version: 1.0.2

Table 6.6.4-5: Estimated worker exposure

		Florasulam	
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Number of applications and application rate:		1 x 0.005 kg a.s./ha	
2 hours/day*, TC potential: 12500 cm ² /person/h TC workwear: 1400 cm ² /person/h TC workwear plus gloves: 1250 cm ² /person/h DFR: 3µg/cm ² foliage per kg a.s./ha DT50 (foliar): 30 days Dermal absorption: 50% Body weight: 60 kg	Potential	0.003	6.3
	Workwear	0.0004	0.7
	Workwear and gloves	0.0003	0.6

*inspection; irrigation

Note: re-entry interval has not been proposed

6.6.4.2 Refinement of generic DFR value (KCP 7.2)

Not required.

6.6.4.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.5 Bystander and resident exposure (KCP 7.2.2)

6.6.5.1 Estimation of bystander and resident exposure

Table 6.6.5-6 shows the exposure model(s) used for estimation of bystander and resident exposure to florasulam. Outcome of the estimation is presented in Table 6.6.5-7. Detailed calculations are in **Appendix 35**.

Table 6.6.5-6: Exposure models for intended uses

Critical use(s)	Winter wheat; Spring barley (max. 0.1L /product/ha)
Model	EFSA on-line calculator OPEX version: 1.0.2

Table 6.6.5-7: Estimated bystander and resident exposure

		florasulam	
Model data	Total absorbed dose (mg/kg/day)	% of systemic AAOEL	% of systemic AOEL
Tractor mounted boom spray application outdoors to low crops Season: Not relevant			

Drift reduction technology: none; Buffer zone: 2-3 m Interval between treatments: NA Minimum volume of water: 200 l <u>florasulam</u> Number of applications and application rate: 1 x 0.005 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days		
<u>Bystanders (adult) BW: 60 kg</u> Drift (95th perc.) Vapour (95th perc.) Deposits (95th perc.) Re-entry (95th perc.)	0.0002 0.0003 5e-05 0.0002	AAOEL has not been allocated for florasulam, thus exposure for residents cover assessment for bystanders
<u>Bystanders (children) BW: 10 kg</u> Drift (95th perc.) Vapour (95th perc.) Deposits (95th perc.) Re-entry (95th perc.)	0.0008 0.0008 0.0001 0.0004	
Residents (adult) BW: 60 kg	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Drift (75th perc.)	8e-05	0.2
Vapour (75th perc.)	0.0003	0.5
Deposits (75th perc.)	2e-05	0.03
Re-entry (75th perc.)	0.0002	0.5
Sum (mean)	0.0005	1
Residents (children)	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Drift (75th perc.)	0.0003	0.7
Vapour (75th perc.)	0.0008	1.6
Deposits (75th perc.)	4e-05	0.08
Re-entry (75th perc.)	0.0004	0.8
Sum (mean)	0.001	2.7

6.6.5.2 Measurement of bystander and/or resident exposure

Since the bystander and/or resident exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for active substance 1 and/or active substance 2 will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of bystander/resident exposure was not necessary and was therefore not performed.

6.6.6 Combined exposure

Not relevant. The product contains only one active substance.

6.6.6.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of Floras 50 SC according to the critical uses is presented in Table 6.6-8. Outcome of the estimation is presented in Table 6.6-9. Detailed calculations are in Appendix 3.

Table 6.6-8: Exposure models for intended uses

Critical uses	Winter wheat (max. 0.1 L product/ha) Spring barley (max. 0.1 L product/ha)
Model	AOEM Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk

	assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015
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Table 6.6-9: Estimated operator exposure – Florasulam

Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Vehicle-mounted Application rate: 0,005 kg a.s./ha			
Cereals			
AOEM Body weight: 70 kg Application volume 200 L/ha	no PPE (mixing/loading/application)	0,8045203	26,82

6.6.7 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mentioned data – even without PPE protection, a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.8 Worker exposure (KCP 7.2.3)

6.6.8.1 Estimation of worker exposure

Table 6.6-10 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with Floras 50 SC according to the critical use(s). Outcome of the estimation is presented in Table 6.6-11. Detailed calculations are in Appendix 3.

Table 6.6-10: Exposure models for intended uses

Critical uses	Winter wheat (max. 0.1 L product/ha) Spring barley (max. 0.1 L product/ha)
Model	AOEM Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-11.1: Estimated worker exposure – Florasulam

Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Number of applications and application rate: max. 0,005 g a.s./ha			
Cereals			
AOEM Outdoor Work rate: 8 hours/day, DT ₅₀ : 4,29 days Initial DFR: 3 µg/cm ² /kg a.s./ha Body weight: 60 kg	no PPE	0,2812500	9,38
	PPE (arm, body and legs covered)	0,0315	1,05

6.6.8.2 Refinement of generic DFR value (KCP 7.2)

No applicable.

6.6.8.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.9 Bystander and resident exposure (KCP 7.2.2)

6.6.9.1 Estimation of bystander and resident exposure

Cereals		
Model data	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Vehicle mounted Application rate: max.: Florasulam 0,005 kg a.s./ha		
Florasulam		
Bystanders (adult) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 60 kg	0,0372325	n.a.
Bystanders (children) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 16,15 kg	0,022811	n.a.
Residents (adult) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 60 kg	0,0386084	1,29
Residents (children) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 16,15 kg	0,0217186	4,34

zRMS Reviewer comment: Model BBA is no longer accepted, thus assessment has been rejected.

Table 6.6-7-2: Estimated bystander and resident exposure—model BREAM BBA

Cereals		
Model data	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Vehicle mounted Application rate: max.: Florasulam 0,0036 kg a.s./ha; 2,4 D 0,18 kg a.s./ha		
Florasulam		
Bystanders (adult) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 60 kg	0,0001154	0,23
Bystanders (children) Buffer strip: 2-3 m; Drift 8,5 % Body weight: 16,15 kg	0,0000901	0,18

6.6.9.2 Measurement of bystander and/or resident exposure

Since the bystander and/or resident exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for Floras 50 SC will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of bystander/resident exposure was not necessary and was therefore not performed.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7.1.1	Krakowian D.	2022	Floras 50 SC: Use of the 3T3 neutral red uptake cytotoxicity test to estimate starting doses for acute oral systemic toxicity tests. Study code: CAO-05-22 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP; Unpublished	N ✕	Elvita Sp. z o.o.
KCP 7.1.4	Krakowian D.	2022	Floras 50 SC In Vitro Skin Corrosion: Reconstructed Human Epidermis (RHE) Test Method. Study code: SCT-02-22 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP; Unpublished	N ✕	Elvita Sp. z o.o.
KCP 7.1.5	Gruszka K.	2022	Floras 50 SC: Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage. Study code: ICE-3-22 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP; Unpublished	N ✕	Elvita Sp. z o.o.
KCP 7.1.6/01	Krakowian D.	2022	Floras 50 SC: In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method. Study code: KST-03-22 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP; Unpublished	N ✕	Elvita Sp. z o.o.
KCP 7.1.6/02	Krakowian D.	2023	Floras 50 SC: In Vitro Skin Sensitisation: Human cell line activation test. Study code: HCLA-03-22 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP; Unpublished	N ✕	Elvita Sp. z o.o.

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

The bridging was not necessary.

Comments of zRMS:	In vitro studies submitted by the applicant to support registration of the product Floras 50 SC has been conducted on the same formulation thus bridging approach is not applicable for this registration process.
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A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Regarding study “ <i>Floras 50 SC: Use of the 3T3 neutral red uptake cytotoxicity test to estimate starting dos-es for acute oral systemic toxicity tests</i> ” Krakowian D., 2022, Reviewer would like indicate that protocol OECD 129 has several limitations are largely due to the differences between whole animal and cell culture systems. Animal and cell culture systems are different with respect to how a substance or toxicant is delivered to the cell and how it is distributed within the cell, metabolized, and excreted. After oral administration, animals must absorb the toxicant from the gastrointestinal tract. The toxicant may or may not be bound to serum proteins, which would reduce its availability to the target organ. The toxicant may be metabolized before, during, and/or after its distribution to the target organs, or the toxicant or its metabolites may be excreted before reaching the target organ. As a consequence, the most critical target organs may not be exposed to the active metabolite, or be exposed for only a limited time or to a relatively small fraction of the administered dose. If a toxicant acts in a specialized organ system in vivo, it may not produce a toxic effect by the same mechanism in cultured cells that are derived from a tissue different from the target organ. For example, a substance that affects a neuroreceptor-mediated pathway in animals would not be expected to produce a similar toxicity in 3T3 or NHK cells; if toxicity is seen in these cell cultures, it may be from a different mechanism or in a different concentration relationship than in vivo. Therefore study has not been accepted and for this endpoint (oral acute toxicity) assessment has been provided based on additivity method ATEmix.
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Reference:	KCP 7.1.1
Report	Floras 50 SC: Use of the 3T3 neutral red uptake cytotoxicity test to estimate starting doses for acute oral systemic toxicity tests, Krakowian D., 2022. Study code: CAO-05-22.
Guideline(s):	OECD Guideline No. 129
Deviations:	<p>The SOP/D/115 has the following deviations from OECD Document No. 129 (ENV/JM/MONO(2010)20). The deviations listed below have been included in the Study Plan:</p> <p>The culture medium recommended by the supplier of cells with the addition of antibiotics and antimycotic mixture was used. This medium contains 5% FBS and 5% NCS instead of 10% NCS. The addition of an antimycotic agent better protects cell cultures against infection. Mentioned changes in the composition of the medium do not adversely affect cell growth.</p> <ul style="list-style-type: none"> • 200 µL of NR medium was used instead of 250 µL, because it is enough volume to carry out the experiment. The dye was used in excess, therefore reducing its amount by 50 µL did not change the results. • Cell washing steps in DPBS after incubation with test item was omitted. In the Łukasiewicz-IPO validation studies, it was shown that each additional rinse causes cell detachment. Therefore, it is safer to omit rinsing.

The complete removal of old buffers / media ensures that residues do not interfere with the further course of the study.

- The two-fold concentrated solution of the test item was added to a well containing 50 µL of culture medium. It was compliant with ICCVAM protocol and the description of the range finder test in ENV/JM/MONO(2010)20.

The following additional steps were added to the method described in the guideline:

- Before seeding of cells, the 96-well plates were coated with poly-L-lysine to facilitate adherence of cells to the bottom of this culture vessel.
- Cell centrifugations (after last rinsing of cells) were added to ensure that as many cells as possible were left in the wells.

GLP: Yes

Acceptability: ~~Yes~~ No

Summary:

NRU in vitro study was performed to estimate starting doses for acute oral systemic toxicity tests. It uses the cytotoxicity assay based on neutral red uptake (NRU) by the 3T3 cell.

Test item: Floras 50 SC

Batch number: RFEAR0501, Production date: 05.04.2022

Test system: 3T3 clone A31 (ECACC 86110401) cell line

Lot. No. 14G021

Study course:

Before main test with two independent runs, the range finder test was carried out.

One day prior to testing 3000 cells were seeded into wells of 96-well plate. Next, the plate was incubated overnight at $37 \pm 1^\circ\text{C}$ in a humidified atmosphere containing $5 \pm 1\%$ CO₂. After treatment with test item and controls, the cells were incubated for a further 2 days. Next, the medium with 25 µg/mL NR dye (Neutral Red) was added to cells and incubated for 3 hours. After incubation, the NR medium was removed, and the cells were carefully rinsed with DPBS. The plates were centrifuged and the buffer was removed. Next, 100 µL desorb solution was added to extract the NR dye. Then, the microplate was shaken in the dark. Finally, the light absorption was measured at 540 nm (OD₅₄₀).

In the main test, the following concentrations of the test item were used with a dilution factor of 3.162: 50 mg/mL, 15.8 mg/mL, 5.0 mg/mL, 1.6 mg/mL, 0.5 mg/mL, 0.2 mg/mL, 0.05 mg/mL, 0.02 mg/mL. Sodium dodecyl sulphate (SDS) was used as a positive control in the final concentration range from 6.8 to 100 µg/mL. The results were compared to vehicle control (only solvent – dilution medium) to calculate cell viability. The IC₅₀ (50% cytotoxicity in vitro) and the expected LD₅₀ (50% mortality in vivo) were calculated according to appropriate mathematical formula.

Results of the studies:

All acceptance criteria (mean absorbance of left and right vehicle control, range of viability, R² for PC, correlation with historical data) were within the appropriate range. Therefore, the experiment is considered as valid.

The mean of IC₅₀ value for two independent runs was 1343.1 µg/mL.

The estimated LD₅₀ value was 1540.5 mg/kg b.w.

Interpretation of the study results:

The test item (Floras 50 SC) should be considered as requiring classification in terms of acute oral toxicity. Thus, other studies (in vivo or in vitro or in silico) are necessary to classify this test item for acute oral toxicity.

An additional study to assess the acute oral toxicity of the plant protection product Floras 50 SC was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements based on calculation method. For confidentiality reasons, calculations/assessment were presented in dRR Part C.

A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (Additivity formula) (for details see Part C). Calculation accepted.
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~~No data on acute dermal toxicity for Floras 50 SC. Studies not submitted, not necessary.~~

~~Results of studies:~~

- ~~— In Vitro Skin Corrosion: Reconstructed Human Epidermis Test Method (OECD 431); (KCP 7.1.4)~~
- ~~— Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage (OECD 438); (KCP 7.1.5).~~

An additional study to assess the acute dermal toxicity of the plant protection product Floras 50 SC was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements based on calculation method. For confidentiality reasons, calculations/assessment were presented in dRR Part C.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (Additivity formula) (for details see Part C). Calculation accepted.
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No data on acute inhalation toxicity for Floras 50 SC. Studies not submitted, not necessary.

The recommended way of spraying formulation Floras 50 SC results in production of medium drops size. Floras 50 SC contains active substance with a vapour pressure below 1×10^{-2} Pa. Thus, according to the regulations (Commission Regulation (EU) No 284/2013), the study of acute inhalation toxicity for Floras 50 SC is not required. Additivity formula to classification was used.

An additional study to assess the acute inhalation toxicity of the plant protection product Floras 50 SC was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements based on calculation method. For confidentiality reasons, calculations/assessment were presented in dRR Part C.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	Study Krakowian D., 2022 based on <i>In Vitro</i> Skin Corrosion OECD 431 three-dimensional RhE method has been reviewed for compliance with the current guidelines, resulting from scientific progress. Study outcome is reliable despite noted deviations from the OECD Guideline. Mentioned deviation is in accordance with the kit manufacturer's protocol and does not affect the results obtained. Study accepted.
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A 2.5.1 Study 1

Reference:	KCP 7.1.4/01
Report	In Vitro Skin Corrosion: Reconstructed Human Epidermis (RHE) Test Method; Krakowian D., 2022. Study code: SCT-02-22
Guideline(s):	OECD Guideline No. 431
Deviations:	The following deviations from the OECD Guideline no. 431, EU Method B.40.BIS were stated (listed in the Study Plan): - permissible variations in temperature, carbon dioxide concentration, humidity and incubation times (according to MatTek protocol). The deviation is to carry out the test under standard laboratory conditions and it does

not affect the results obtained. The concentration of carbon dioxide (CO₂) in the incubator decreased once to the level below 4.0%.

- The acceptance criterion for the difference in viability of tissues exposed to the test item has been changed. According to OECD guideline 431, a coefficient of variation (CV) would have to be calculated, which should not be greater than 30%. However, according to the kit manufacturer's recommendations (MatTek protocol), the appropriate criterion for two tissues is to calculate the difference in viability between them (this difference should not exceed 30%), as is the case in the other RHE methods listed in OECD guideline 431. This deviation is in accordance with the kit manufacturer's protocol and does not affect the results obtained.

GLP: Yes

Acceptability: Yes

Summary:

In Vitro Skin Corrosion test method was performed in order to obtain information on health hazards resulting from an influence of the test item on the reconstructed human epidermis. The study addresses the human health endpoint skin corrosion.

Test item: Floras 50 SC

date of production: 05.04.2022. Batch No. RFEAR0501

Test system: EpiDerm™ kit (MatTek In Vitro Life Science Laboratories in Bratislava).

Study course:

Skin corrosion refers to the production of irreversible tissue damage following the application of a test item. The test consists of a topical exposure of the neat test item to a human reconstructed epidermis model followed by a cell viability test. Cell viability is measured by dehydrogenase conversion of MTT, present in cell mitochondria, into a blue formazan salt that is quantitatively measured after extraction from tissues. The percentage reduction of cell viability in comparison of untreated negative controls is used to predict the skin corrosion potential.

Two inserts with tissues of the human skin model EpiDerm™ were treated with the test item for 3 minutes and for 60 minutes. The test item was applied directly to each tissue and spread to match the tissue size.

Deionized water was used as negative control and 8N KOH solution was used as positive control.

Results of the studies:

All acceptance criteria (absorbance value for negative control, mean value of relative tissue viability of positive control, variation within the tissue replicates, compliance with historical data) were within the appropriate range. Therefore, the experiment is considered as valid.

After the 3-minute exposure to the test item, the mean value of relative tissue viability was equal to 102%. After the 1-hour exposure to the test item, the mean value of relative tissue viability was equal to 83.7%. These values are above the threshold of non-corrosive effects on the skin (viability ≥ 50 % after 3-minutes exposure and ≥ 15 % after 60-minutes exposure).

Interpretation of the study results:

The test item, Floras 50 SC, is identified as non-corrosive in the Reconstructed human Epidermis (RHE) test method. It cannot be classified as category 1 in the UN GHS classification. Therefore, further testing on skin irritation potential with another suitable *in vitro* study may be required to classify this test item.

An additional study to assess the skin irritation of the plant protection product Floras 50 SC was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements based on calculation method. For confidentiality reasons, calculations/assessment were presented in dRR Part C.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Study Gruszka K., 2022. <i>In vitro</i> ICE test method an organotypic model has been reviewed for compliance with the current guidelines. Noted deviation has no impact on final study outcome, thus study results are reliable. Study accepted
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~~None of ingredients of formulation Floras 50 SC have classification and/or potential to eye irritation.~~

A 2.6.1 Study 1

Reference:	KCP 7.1.5/01
Report	Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage; Gruszka K., 2022. Study code: ICE-03-22
Guideline(s):	OECD Guideline No. 438
Deviations:	Due to confusing entries in the guideline (suggesting a typing error), the categorization was based on the criteria contained in the drafts for guidelines. These are criteria originally developed by Cazelle et al (2014) and adopted by the OECD.
GLP:	Yes
Acceptability:	Yes

Summary:

The isolated chicken eye (ICE) test was performed in order to obtain information on health hazards resulting from a superficial influence of the test item on the eye.

Test item: Floras 50 SC

Test system: Chicken eyeballs

Study course:

Undamaged chicken eyes (corneal opacity ≤ 0.5 , fluorescein retention ≤ 0.5) with similar thickness ($\pm 10\%$) were placed in superfusion apparatus ($32 \pm 1.5^\circ\text{C}$ with saline drops).

The test item and the material used in the positive control (benzalkonium chloride) were applied uniformly over the surface of the cornea in amount of 0.03 mL, while the material used in the negative control (saline) was applied in volume of 0.03 mL. Then they were rinsed with saline.

Three eyeballs were used for the test item and three for each control item.

The corneas treated with the test item and the control items were evaluated prior to treatment and at 30, 75, 120, 180, and 240 minutes (± 5 minutes) after the post-treatment rinse. At all observation time points, corneal opacity and swelling were evaluated, whereas morphological changes of the corneal surface were recorded. The quantitative determination of fluorescein retention was performed only prior to treatment and 30 minutes after the end of the exposure.

After final evaluation, the eyeballs were fixed in a 4% formaldehyde solution for histopathological evaluation.

Results of the studies:

For eyeballs treated with the test item:

- the mean fluorescein retention value was equal to 0.0 (ICE class I),
- the maximum mean corneal opacity value was equal to 0.5 (ICE class I),
- the maximum mean corneal swelling value was equal to -14.8% (ICE class I),
- test item on the surface was not observed.

Histopathological examinations were not able to classify test item as category 1.

Interpretation of the study results:

On the grounds of the study results described in this Report and the overall in vitro Irritancy Classification, it may be stated that the test item, i.e. Floras 50 SC should not have a negative effect. According to UN GHS classification criteria no prediction can be made, since the ICE Class combination of

the 3 endpoints were: 3 x I (no category). Based on the results obtained during the histopathological evaluation, it can be concluded that the test item should not have a negative effect on the cornea of chickens in the ICE test. The test item can be put into “no category”.

The other additional researches (in vivo or in vitro) are not necessary for classification of this test item.

A 2.7 Skin sensitisation (KCP 7.1.6)

Reviewer general comment regarding skin sensitisation assessment:

There are two *in vitro* studies has been submitted to elucidate skin sensitisation potential of the product Floras 50 SC. Both studies gave clear negative results.

Study 1 *In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method*; Krakowian D., 2022. has been used to assess AOP key event 2 (events in Keratinocytes) of the pathways and the intermediate steps associated with skin sensitization.

Study 2 *In Vitro Skin Sensitisation: Human cell line activation test*; Krakowian D., 2023 has been used to assess AOP key Event 3 (events in Dendritic cell) of the pathways and the intermediate steps associated with skin sensitization

Outcome of the both studies allow to conclude that the test item do not be considered as potentially skin sensitizing.

Comments of zRMS:	Study Krakowian D., 2022 <i>In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method</i> has been reviewed for compliance with the current guidelines.. Deviations from the protocol noted by the study director, regarding an alternative luminescence measurement, have been adequately explained. zRMS Reviewer is in the opinion that this deviation does not affect the test results as the cell viability obtained is referenced to the negative control and considered as reliable data. Study accepted.
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~~None of ingredients of formulation Floras 50 SC have classification and/or potential to skin sensitization.~~

A 2.7.1 Study 1

Reference: KCP 7.1.6/01

Report In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method; Krakowian D., 2022.
Study code: KST-03-22

Guideline(s): OECD Guideline No. 442D

Deviations: The following deviations from OECD TG no. 442D and EU Method B.60 are stated (listed in the Study Plan):

- an alternative luminescence measurement is used. This is related to the use of another microplate reader than described in the guideline. Nevertheless, control experiments (validation study) were carried out, which were successfully completed;
- the cytotoxicity assay was performed according to the validation protocol DB-ALM no. 155 with additional reference wavelength. According to this protocol, the MTT concentration in the medium is 0.6 mg/mL instead of 5 mg/mL. Isopropanol was used instead of the SDS solution to extract the formazan, because it is a faster and safer way of detection. Absorbance should be measured at 570 nm as this is the more appropriate wavelength for formazan dissolved in isopropanol. The additional use of the reference wavelength (690 nm) is an improvement in the measurement, as it eliminates the background signal (plastic bottom of the plate, cells, unrinsed

material deposited on the bottom). This deviation does not affect the test results as the cell viability obtained is referenced to the negative control;
- the permissible range of carbon dioxide concentration in the incubator and the permissible range of incubation times have been added so that the test can be performed under laboratory conditions.
The above deviations do not affect the course and results of the study.

GLP: Yes
Acceptability: Yes

Summary:

In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method was performed to investigate the potential of the test item to sensitize the skin by using the KeratinoSens™ cell line.

Test item: Floras 50 SC

date of production: 05.04.2022 Batch No. RFEAR0501

Test system: KeratinoSens™ (Givaudan)

Study course:

The ARE-Nrf2 luciferase test method makes use of an immortalised adherent cell line named KeratinoSens™. The cell line contains the luciferase gene under the transcriptional control of a constitutive promoter fused with an ARE from a gene that is known to be up-regulated by contact sensitizers. This allows quantitative measurement (by luminescence detection) of luciferase gene induction. The measured endpoint is the up-regulation of luciferase activity after 48 hours of incubation with test item. Simultaneously, cell viability is measured by MTT cytotoxicity assay.

A stock solution containing 40 mg/mL test item in DMSO was prepared, and used to prepare a two-fold dilutions (12 concentrations). These concentrations were further diluted to obtain following final concentrations: 0.195 µg/mL, 0.39 µg/mL, 0.78 µg/mL, 1.56 µg/mL, 3.125 µg/mL, 6.25 µg/mL, 12.5 µg/mL, 25 µg/mL, 50 µg/mL, 100 µg/mL, 200 µg/mL, 400 µg/mL.

Trans-cinnamaldehyde was used as positive control in the final concentration range from 4 to 64 µM.

To determine the skin sensitization potential of the test item, two independent and valid runs were performed. The results were compared to negative control (only solvent).

Results of the studies:

All acceptance criteria (luciferase activity induction, and EC1.5 value for PC, the average CV of the luminescence reading for NC) were within the appropriate range. Therefore, the experiment is valid.

After the treatment with the test item:

- the overall IC50 could not be calculated (IC50 was calculated only for the first run, and equal to 391.6 µg/mL) and IC30 was equal to 245.5±13.7 µg/mL
- the overall maximal fold induction of luciferase activity (oImax) value for two independent runs was 1.2,
- the overall EC1.5 could not be calculated,
- in both runs the viability of cells above 70% (based on IC30) for the lowest concentration, in which 1.5-fold induction of luciferase activity was noted (EC1.5 concentration) could not be calculated,
- the clear concentration-response relationship for the luciferase activity was not observed for both runs.

Interpretation of the study results:

In two independent runs, none of the requirements for positive results were met. Therefore, it can be concluded that the test item is negative in the KeratinoSens assay, and should not be considered as potentially skin sensitizing. However, this is only one of the key events in the skin sensitisation process, so additional tests may be required to fully classify the item.

Comments of zRMS:	Study <i>In Vitro Skin Sensitisation: Human cell line activation test</i> ; Krakowian D., 2023 has been reviewed for compliance with the current guidelines. Deviations from the protocol noted by the study director, have been adequately explained and has no impact on study outcome. Study accepted.
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A 2.7.2 Study 2

Reference:	KCP 7.1.6/02
Report	In Vitro Skin Sensitisation: Human cell line activation test; Krakowian D., 2023. Study code: HCLA-03-22
Guideline(s):	OECD Guideline No. 442E
Deviations:	The following deviations from OECD TG no. 442E are stated (listed in SOP/D/113): <ul style="list-style-type: none">• Maintenance medium without mercaptoethanol and with the addition of glutamine is used for the culture of THP-1 cells. This deviation does not affect the obtained results, which was confirmed by the validation study, in which the correct results of reference materials were obtained.• The permissible range of carbon dioxide concentration in the incubator and the permissible range of temperatures have been added so that the test can be performed under laboratory conditions. This deviation does not affect the obtained results, which was confirmed by the validation study, in which the correct results of reference materials were obtained. The above deviations do not affect the course and results of the study.
GLP:	Yes
Acceptability:	Yes

Summary:

The in vitro Human cell line activation test was performed to assess the sensitizing potential of the test item, by quantifying changes in the expression level of the two cell surface markers CD86 and CD54.

Test item: Floras 50 SC

date of production: 05.04.2022. Batch No. RFEAR0501

Test system: THP-1 cells (300356 lot. 300356-1714SF)

Study course:

The h-CLAT method quantifies changes of cell surface marker expression (i.e. CD86 and CD54) on a THP-1 cells, following 24 hours exposure to the test item. The changes of surface marker expression were measured by flow cytometry following cell staining with fluorochrome-tagged antibodies. Cytotoxicity measurement (PI uptake) was also conducted concurrently to assess whether upregulation of surface marker expression occurs at sub-cytotoxic concentrations. The RFI of surface markers were calculated and used in the prediction model to support the discrimination between sensitizers and non-sensitizers.

Prior to testing, the solubility of the test item in medium was determined and medium (RPMI 1640 with 25 mM HEPES) was chosen as the solvent. Therefore, the medium control was used as a reference for the test item. A range finder test was then performed to determine the concentration of CV75. In the first range finder assay the CV75 was not determined, so another test was conducted with different concentration of the test item. In that test CV75 was equal to 3132.6 µg/mL, so the highest final concentration of the test item in the main test was 3760 µg/mL and a geometric series (factor 1.2) of 7 dilutions was prepared from this stock solution (3760 µg/mL; 3133.3 µg/mL; 2611.1 µg/mL; 2175.9 µg/mL; 1813.3 µg/mL; 1511.1 µg/mL; 1259.2 µg/mL; 1049.3 µg/mL). DNCB (2.5 µg/mL) was used as positive control with DMSO as solvent control.

Results:

Three independent runs were carried out, as the first run did not meet the acceptance criteria (first experiment was found invalid). In run 2 and 3 all acceptance criteria were met, therefore, the study was considered valid.

Two valid runs produced negative results (RFIs for CD86 and CD 54 were below 150 and 200, respectively). Therefore, according to the h-CLAT prediction model the result of this study is negative. EC150 and EC200 could not be calculated.

Interpretation of the study results:

It can be concluded that, under the experimental conditions of this study, the test item has no ability to activate dendritic cells (one of the four key events in skin sensitisation) and therefore should not be considered as potentially skin sensitizing. However, this is only one of the key events in the skin sensitisation process, so additional tests may be required to fully classify the item.

A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co- formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.9.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

Comments of zRMS:	Default values of dermal absorption proposed by the Applicant for PPP Floras 50SC has been incorrectly entered. Based on Guidance on Dermal Absorption (EFSA Journal 2017;15(6)4873) for concentrate and spray dilution it must be 10% and 50% respectively (Formulation types: soluble concentrate (SL), sus-pension concentrate (SC), flowable concentrate for seed treatment (FS), flowable (FL) (=SC)). Due to Applicants' mistake, zRMS decided to provide new NDE assessment.
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According requirements from Reg. No. 284/2013/WE the study shall be conducted when dermal exposure is a significant exposure route and no acceptable risk is estimated using default absorption value. In order to make assessment of exposure, for Floras 50 SC has proposed a default dermal absorption value of ~~25~~ **10%** for the concentrate and ~~75~~ **50 %** for the spray solution, based on Guidance on Dermal Absorption (EFSA Journal 2017;15(6)4873).

Use of plant protection product Floras 50 SC is safe for operator, taking into account proposed dose of product, type of usage, type of personal protective equipment (gloves, protective garment and sturdy footwear). Using vehicle mounted sprayer and maintain general rules of safety and hygiene of working with plant protection products and comply with requirements enclosed in label, risk during employ Floras 50 SC is acceptable, absorbed dose have safe value, below AOEL for this active ingredient. According to above there isn't necessity to do tests of dermal absorption for Floras 50 SC.

A 2.11 Other/Special Studies

No additional studies.

Appendix 3 — Exposure calculations

Entry Data:

Substance name	Florasulam
Product name	Floras 50 SC
Reference value non-acutely toxic active substance (RVNAS)	0.05 mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	mg/kg bw/day
Crop type	Cereals
Substance properties	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Minimum volume water for application (liquids)	100 L/ha
Maximum application rate of active substance	0.005 kg a.s. /ha
50% Dissipation Time DT50	4.29 days
Initial Dislodgeable Foliar Residue	3 µg/cm ² of foliage/kg a.s. applied/ha
Dermal absorption of product	25.00%
Dermal absorption of in-use dilution	75.00%
Oral absorption of active substance	100.00%
Inhalation absorption of active substance	100.00%
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa
Scenario	
Indoor or Outdoor application	Outdoor
Application method	Downward spraying
Application equipment	Vehicle-mounted
Buffer strip	2-3 m
Number of applications	1
Interval between multiple applications	365 days
Season (upward spraying orchards only)	not relevant

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

Operator exposure for Floras 50 SC outdoor spray applications

Application rate of active substance	0.005 kg a.s./ha	<i>i_AppRate</i>
Assumed area treated	50 ha/day	<i>d_AreaTreated</i>
Amount of active substance applied	0.25 kg a.s./day	<i>i_AmountAS</i>
Dermal absorption of the product	25.00%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	75.00%	<i>i_AbsorInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment	
		75 th centile	95 th centile			
Mixing and loading	Hands	1671	6047	AOEM		
	Body	1346	48147	AOEM		
	Head	13	71	AOEM		
	Protected hands (gloves)	14	50	AOEM		
	Protected body (workwear or protective garment and sturdy footwear)	7	37	AOEM		
	Protected head (hood and face shield)	0	4	AOEM		
	Inhalation	2	28	AOEM		
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor	
	Gloves	No				
	Clothing	Potential exposure		Incl. in AOEM model		
Application	Head and respiratory PPE	None		1	1	
	Water soluble bag	No		1		
		Exposure values	µg exposure/day applied		Reference	Comment
			75 th centile	95 th centile		
		Hands	37	84	AOEM	
		Body	21	107	AOEM	
		Head	1	3	AOEM	
		Protected hands (gloves)	20	2835	AOEM	
		Protected body (workwear or protective garment and sturdy footwear)	1	1	AOEM	
		Inhalation	1	1	AOEM	
Protective Equipment		Select for inclusion		Penetration factor	Inhalation Protection factor	
Gloves	No					
Clothing	Potential exposure		Incl. in AOEM model			
Head and respiratory PPE	None		1	1		
Closed cab	No		vehicle mounted upward spraying only			

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.8045203	0.8045203	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0134087	0.0134087	
% of RVNAS	26.82%	26.82%	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

Worker exposure from residues on foliage for Floras 50 SC				
Crop type	Cereals			
Indoor or outdoor	Outdoor			
Application method	Downward spraying			
Application equipment	Vehicle-mounted			
Worker's task	Inspection, irrigation			
Main body parts in contact with foliage	Hand and body			
Application rate of active substance	0.005	kg a.s./ha		i_AppRate
Number of applications	1			i_AppNo
Interval between multiple applications	365	days		i_AppInt
Half-life of active substance	4.29	days		d_HalfLifeAS
Multiple application factor	1.0			d_MAF
Dermal absorption of the product	25.00%			i_AbsorpProduct
Dermal absorption of the in-use dilution	75.00%			i_Absorplnuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.015	µg a.s./cm ²		d_DFR
Working hours	2	hr		d_WorkHr
Dermal transfer coefficient - Total potential exposure	12500	cm ² /hr		d_DermTcUCV
Dermal transfer coefficient - arms, body and legs covered	1000	cm ² /hr		d_DermTcCV1
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment			d_DermTcCV2
Inhalation transfer coefficient for automated applications	NA	ha/hr*10 ⁴ (-3)		d_InhalTcAut
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10 ⁴ (-3)		d_InhalTcCut
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10 ⁴ (-3)		d_InhalTcSort
1. Total				
	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0.2812500	0.0315000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0046875	0.0005250		
% of RVNAS	9.38%	1.05%		

A 3.3 Bystander and resident exposure calculations (KCP 7.2.2.1)

Bystander exposure for Floras 50 SC				
Crop type	Cereals			
Application method	Downward spraying			
Application equipment	Vehicle-mounted			i_AppEquip
Formulation type	Water-soluble concentrates, emulsifiable concentrate, etc.			
Application rate of the product	0.005 kg a.s./ha			i_AppRate
Buffer strip	2-3 m			i_Buffer
Concentration of active substance (in-use dilution for liquid applications)	0.05 g a.s./l			d_ConcAS
Dermal absorption of product	25.00%			i_AbsorpProduct
Dermal absorption of in-use dilution	75.00%			i_AbsorpInuse
Oral absorption	100.00%			i_AbsorpOrallInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.015 µg a.s./cm ²			d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa			i_Volat
Concentration in air	0.001 mg/m ³			d_AirCon
Bystander dermal spray drift exposure - adult	1.21 ml spray dilution/person			
Bystander dermal spray drift exposure - child	0.74 ml spray dilution/person			
Bystander inhal. spray drift exposure - adult	0.00050 ml spray dilution/person			
Bystander inhal. spray drift exposure - child	0.00112 ml spray dilution/person			
Exposure duration	2 hours			d_ByExpDur
Exposure duration entry into treated crops	0.25 hours			d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%			d_ClothAF
Breathing rate adult	0.23 m ³ /kg bw/day			d_BreathRAAd
Breathing rate child (1-3 year old)	1.07 m ³ /kg bw/day			d_BreathRCh
Drift percentage on surface (90th percentile)	8.50%			
Turf transferable residues percentage	100%			d_Turf
Transfer coeff. of surface deposits-adult	14000 cm ² /hour			d_ByTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	5200 cm ² /hour			d_ByTCCh
Saliva extraction percentage	50.00%			d_SalExt
Surface area of hands mouthed	20 cm ²			d_AreaHM
Frequency of hand to mouth activity	20 events/hour			d_ByFreqHM
Ingestion rate for mouthing of grass per day	25 cm ²			d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%			d_DRP
Transfer coefficient for entry into treated crops - adult	7500 cm ² /h			d_TcEntryAd
Transfer coefficient for entry into treated crops - child	2250 cm ² /h			d_TcEntryCh
1. Total				
1.1 1-3 year old child				
	Spray drift	Vapour	Surface deposits	Entry into treated crops
Total systemic exposure (mg a.s./day)	0.0228110	0.0107000	0.0017638	0.0063281
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0022811	0.0010700	0.0001764	0.0006328
% of RVAAS	#DZIEL/0!	#DZIEL/0!	#DZIEL/0!	#DZIEL/0!
1.2 Adult				
	Spray drift	Vapour	Surface deposits	Entry into treated crops
Total systemic exposure (mg a.s./day)	0.0372325	0.0138000	0.0046219	0.0216338
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0006205	0.0002300	0.0000770	0.0003516
% of RVAAS	#DZIEL/0!	#DZIEL/0!	#DZIEL/0!	#DZIEL/0!

Resident exposure for Floras 50 SC						
Application type	Cereals					
Application method	Downward spraying					
Application equipment	Vehicle-mounted					
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.					
Buffer strip	2-3 m					
Application rate of the product	0.005 kg a.s./ha					
Concentration of active substance (in-use dilution for liquid applications)	0.05 g a.s./l					
Dermal absorption of product	25.00%					
Dermal absorption of in-use dilution	75.00%					
Oral absorption	100.00%					
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.015 µg a.s./cm²					
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa					
Concentration in air	0.001 mg/m³					
Resident dermal spray drift exposure 75th percentile - adult	0.47 ml spray dilution/person					
Resident dermal spray drift exposure 75th percentile - child	0.327 ml spray dilution/person					
Resident inhal. spray drift exposure 75th percentile - adult	0.00010 ml spray dilution/person					
Resident inhal. spray drift exposure 75th percentile - child	0.00022 ml spray dilution/person					
Resident dermal spray drift exposure mean - adult	0.22318 ml spray dilution/person					
Resident dermal spray drift exposure mean - child	0.18 ml spray dilution/person					
Resident inhal. spray drift exposure mean - adult	0.00009 ml spray dilution/person					
Resident inhal. spray drift exposure mean - child	0.00017 ml spray dilution/person					
Exposure duration dermal	2 hours					
Exposure duration inhalation	24 hours					
Exposure duration entry into treated crops	0.25 hours					
Light clothing adjustment factor	18.0%					
Breathing rate adult	0.23 m³/day/kg					
Breathing rate child (1-3 year old)	1.07 m³/day/kg					
Drift percentage on surface (75th percentile)	5.60%					
Drift percentage on surface (mean)	4.10%					
Turf transferable residues percentage	5.00%					
Transfer coeff. of surface deposits-adult	7300 cm²/hour					
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm²/hour					
Saliva extraction percentage	0.00%					
Surface area of hands mouthed	20 cm²					
Frequency of hand to mouth activity	5 events/hour					
Ingestion rate for mouthing of grass per day	25 g/day					
Dislodgeable residues percentage transferability for object to mouth	20.00%					
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500 cm²/h					
Transfer coefficient for entry into treated crops (75th percentile) - child	2250 cm²/h					
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm²/h					
Transfer coefficient for entry into treated crops (mean) - child	1794 cm²/h					
1. Total						
1.1 1-3 year old child						
Spray drift (75th percentile)		Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)	
Total systemic exposure (mg a.s./day)		0.0100663	0.0107000	0.0005866	0.0063281	0.0217186
Total systemic exposure per kg body weight (mg/kg bw/day)		0.0010066	0.0010700	0.0000587	0.0006328	0.0021719
% of RVNAS		2.01%	2.14%	0.12%	1.27%	4.34%
1.2 Adult						
Spray drift		Vapour	Surface deposits	Entry into treated crops	All pathways (mean)	
Total systemic exposure (mg a.s./day)		0.0144575	0.0138000	0.0015330	0.0210938	0.0306084
Total systemic exposure per kg body weight (mg/kg bw/day)		0.0002410	0.0002300	0.0000256	0.0003516	0.0006435
% of RVNAS		0.48%	0.46%	0.05%	0.70%	1.29%

Estimation of bystander and resident exposure (adults and children)				
Active substance (a.s.)		Florasulam		
Product		Floras 50 SC		
Intended uses		Field Crops, Tractor Mounted (FCTM)		
Treated area per day (A)	20	ha/d		
Application rate (AR)	0.005	kg a.s./ha		
Number of applications (NA)	1	1)		
1) Consideration of more than two applications are not necessary if degradation of the active substance on foliage of at least 50 % can be assumed between two applications (otherwise use multiple application factor).				
Dermal absorption (DA)	50	% (worst case, e.g. during application)		
Inhalation absorption (IA)	100	%		
Oral absorption (OA)	100	%		
Systemic AOEL	0.05	mg/kg bw/d		
Body weight (BW)	60	kg/person (adults)		
	16.15	kg/person (children)		
Bystander exposure towards Florasulam				
Adults		Children		
Bystander: Dermal exposure after application in (via spray drift)				
$SDE_B = (AR \times D \times BSA \times DA) / BW$		$SDE_B = (AR \times D \times BSA \times DA) / BW$		
$(0.5 \times 2.77\% \times 1 \times 50\%) / 60$		$(0.5 \times 2.77\% \times 0.21 \times 50\%) / 16.15$		
External exposure	0.01385 mg/person	External exposure	0.0029085	mg/person
External exposure	0.00023083 mg/kg bw/d	External exposure	0.00018009	mg/kg bw/d
Absorbed dose:	0.0001154 mg/kg bw/d	Absorbed dose:	0.0000900	mg/kg bw/d
Bystander: Inhalation exposure after application in				
$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$		$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$		
$(0.000 / 360 \times 0.005 \times 20 \times 5 \times 100\%) / 60$		$(0.000 / 360 \times 0.005 \times 20 \times 5 \times 100\%) / 16.15$		
External exposure	1.3889E-06 mg/person	External exposure	7.9021E-07	mg/person
External exposure	2.3148E-08 mg/kg bw/d	External exposure	4.9425E-08	mg/kg bw/d
Absorbed dose:	0.0000000 mg/kg bw/d	Absorbed dose:	0.0000000	mg/kg bw/d
Total systemic exposure: $SE_B = SDE_B + SIE_B$		Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure (absorbed dose)	0.00692639 mg/person	Total systemic exposure (absorbed dose)	0.00145505	mg/person
Total systemic exposure (absorbed dose)	0.0001154 mg/kg bw/d	Total systemic exposure (absorbed dose)	0.0000901	mg/kg bw/d
% of AOEL:	0.23 %	% of AOEL:	0.18	%

Appendix 4 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)

No additional data.

Appendix 5 Detailed NDE assessment provided by the zRMS Reviewer

Exposure assessment for operator, worker, resident and bystander

Product: Floras 50 SC
OPEX version: 1.0.2
29 April 2024

Information on product and active substance(s)

Product name	Floras 50 SC
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Herbicide
Name of active substance	Florasulam
Concentration of active substance [g a.s./l or kg]	50
AOEL [mg/kg bw/day]	0.05
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	10





7 Assessed uses

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	0.1	l/ha	1	NA	200	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	2-3	0





8 Operator

8.1 Use 1 : Field crops

Short term exposure

Mixing/loading	Application	Florasulam (% AOEL) Normal & vehi- cle-mounted
		16.6
		12

Acute exposure

Mixing/loading	Application	Florasulam (% AOEL) Normal & vehi- cle-mounted
		
		

8.1.1 Scenario 1 : Outdoor, normal, downward spraying, vehicle-mounted

8.1.1.1 Summary data - Short term exposure

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Number of applications and application rate: 1 x 0.005 kg a.s./ha Dermal absorption (concentrate): 10 % Dermal absorption (in-use dilution): 50 %			
Florasulam	M/L: Workwear App: Workwear	0.006	12

8.1.1.2 Summary data - Acute exposure

Model data	Level of PPE	Total absorbed dose [mg/kg bw]	% of systemic AA- OEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/95th percentile Crop density: Normal			
Number of applications and application rate: 1 x 0.005 kg a.s./ha Dermal absorption (concentrate): 10 % Dermal absorption (in-use dilution): 50 %			
Florasulam	M/L: Workwear + Protected hands + FP2, P2 and similar App: Workwear + Protected hands + FP2, P2 and similar		No results!

9 Worker

9.1 Use 1 : Field crops

9.1.1 Scenario 1 : Outdoor, normal

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: NA Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h			
Number of applications & application rate: 1 x 0.005 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50 Foliar: 30 days DT50 Air: 30 days DT50 Soil: 30 days			
Potential	0.003	6.3	0
Workwear	0.0004	0.7	0
Workwear and gloves	0.0003	0.6	0
Hands covered, no workwear			

10 Resident

10.1 Use 1 : Field crops

10.1.1 Scenario 1 : Outdoor, season not relevant

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: NA Minimum volume of water: 200 l			
Number of applications and application rate: 1 x 0.005 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Florasulam			
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0003	0.7
	Vapour (75th perc.)	0.0008	1.6
	Deposits (75th perc.)	4e-05	0.08
	Re-entry (75th perc.)	0.0004	0.8
	Sum (mean)	0.001	2.7
Resident adult Body weight: 60 kg	Drift (75th perc.)	8e-05	0.2
	Vapour (75th perc.)	0.0003	0.5
	Deposits (75th perc.)	2e-05	0.03
	Re-entry (75th perc.)	0.0002	0.5
	Sum (mean)	0.0005	1

11 Bystander

11.1 Use 1 : Field crops

11.1.1 Scenario 1 : Outdoor, season not relevant

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AAOL
Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: NA Minimum volume of water: 200 l			
Number of applications and application rate: 1 x 0.005 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Florasulam			
Bystander child Body weight: 10 kg	Drift (95th perc.)	0.0008	
	Vapour (95th perc.)	0.0008	
	Deposits (95th perc.)	0.0001	
	Re-entry (95th perc.)	0.0004	
Bystander adult Body weight: 60 kg	Drift (95th perc.)	0.0002	
	Vapour (95th perc.)	0.0003	
	Deposits (95th perc.)	5e-05	
	Re-entry (95th perc.)	0.0002	

12 Appendix

12.1 Operator

12.1.1 Use 1 : Field crops

12.1.1.1 Scenario 1 : Outdoor, normal, downward spraying, vehicle-mounted

Florasulam , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	Name of active substance	Florasulam
Concentration of active substance [g a.s./l or kg]	50	Crops	Field crops
Area treated [ha/day]	50	Application method	Downward spraying
Dermal absorption [%] (concentrate)	10	Application technique	Vehicle-mounted
Dermal absorption [%] (dilution)	50	Indoor/outdoor	Outdoor
Oral absorption [%]	100	Drift reduction [%]	0
Inhalation absorption [%]	100	Type of cultivation	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.05		
AAOEL [mg/kg bw]			

Florasulam , Per body part - Short term exposure

Activity	Systemic exposure per body part	With work-wear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	<i>Hand protection</i>	<i>None</i>	<i>None</i>
	Hands exposure	5.6	5.6
	<i>Body protection</i>	<i>Workwear</i>	<i>Workwear</i>
	Body exposure	0.04	0.04
	<i>Head protection</i>	<i>None</i>	<i>None</i>
	Head exposure	0.03	0.03
	<i>Inhalation protection</i>	<i>None</i>	<i>None</i>
	Inhalation exposure	0.03	0.03
Application (µg/kg bw per day)	<i>Hand protection</i>	<i>None</i>	<i>None</i>
	Hands exposure	0.3	0.3
	<i>Body protection</i>	<i>Workwear</i>	<i>Workwear</i>
	Body exposure	0.005	0.005
	<i>Head protection</i>	<i>None</i>	<i>None</i>
	Head exposure	0.008	0.008
	<i>Inhalation protection</i>	<i>None</i>	<i>None</i>
	Inhalation exposure	0.009	0.009
Total	Total systemic exposure [mg/kg bw per day]	0.006	0.006
	% of AOEL	12	12

12.2 Worker

12.2.1 : Field crops

12.2.1.1 Scenario 1 : Outdoor, normal

Florasulam , Input data

Indoor/outdoor	Outdoor	AOEL [mg/kg bw/day]	0.05
Re-entry activity	Inspection, irrigation	Dermal transfer coefficient - Total potential exposure [cm²/h]	12500
Crops	Field crops	Dermal transfer coefficient - Arm, body and legs covered [cm²/h]	1400
Application method	Downward spraying	Dermal transfer coefficient - Hands, arm, body and legs covered [cm²/h]	1250
Application technique	Vehicle-mounted	Dermal transfer coefficient - Hands covered, no work- wear [cm²/h]	
Max. application rate of the product [l or kg/ha]	0.1	DFR refined worker [µg/cm² foliage per kg a.s./ha]	3
Max. no. of applications	1	DT50 foliar worker [days]	30
Interval between multiple applications [days]	NA		
Multiple application factor	1		
Body weight (kg)	60		

Name of active substance	Florasulam
Dermal absorption [%] (dilution)	50
Inhalation absorption [%]	100
Time [hours per day]	2

Florasulam , Exposure per body part

Exposure route	Description	Potential	Workwear	Workwear and gloves	Gloves
Dermal	Systemic dermal exposure [mg a.s. per day]	0.2	0.02	0.02	NA
Inhalation	Systemic inhalation exposure [mg a.s. per day]				NA
Total	Total systemic exposure [mg a.s. per day]	0.2	0.02	0.02	NA
	Total systemic exposure [mg/kg bw per day]	0.003	0.0004	0.0003	NA
	% of AOEL	6.3	0.7	0.6	NA